Modelling Salmonella phage production in a bioreactor

SÍLVIO B. SANTOS, J. AZEREDO AND E.C. FERREIRA
IBB- Institute for Biotechnology and Bioengineering, Centre of Biological Engineering, University of Minho, Campus de Gualtar, 4710-057 Braga, Portugal

ABSTRACT

In recent years, the interest in phages has increased not only because of their potential use as alternatives to antibiotics (phage therapy) but also on account of their applications in many other fields (phage display, immunology, microbial genetics, diagnostics, vaccine development, biosensors, etc.). In all these applications it is important to obtain large amounts of phage and thus prediction, control and optimization of phage production will play an important role.
Mathematical models have been used for studying the dynamics of bacteriophages and, more recently, to evaluate its applicability in phage therapy. The utility of simple models is to identify, in a quantitative way, the dominant factors that contribute to the population dynamics and to the evolution of the interactions between bacteria and phage and consequently they can also be used to predict, control and optimize phage production.
Salmonella has long been recognized as an important zoonotic pathogen of economic significance in animals and humans and remains the primary cause of reported food poisoning worldwide with massive outbreaks seen in recent years where *Salmonella enteritidis* is the most commonly reported serovar. Consequently, the use of salmonella phages are of great value and thus production of this phage constitutes a good case of study.
The goal of this work was the development of a population dynamic model that predicts the interaction between a Salmonella phage and its respective host. Simulated data generated by the model was compared with the values obtained experimentally allowing to assess the suitability of the model. To obtain the experimental data phage was added at low MOI (Multiplicity Of Infection) to a growing liquid culture of bacterial cells in initial exponential phase and samples were taken for phage, bacteria and carbon source concentration.
The suitability of the model was firstly assessed for small volumes but it is expected that the model may help the optimization of phage production and thus, a scale up of phage production was carried on in a 5L fermenter and results were compared with the simulated data. The phage-bacteria system had similar behaviour and the simulation had a good correlation with the experimental results. From the results we conclude that the model can be used to predict and to optimize the amount of phage obtained in the production process.